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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/226,794	01/07/1999	WALDEMAR DEBINSKI	6460-4	9546

7590

12/11/2002

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EXAMINER

UNGAR, SUSAN NMN

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 12/11/2002

28

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/226,794

Applicant(s)

Debrinski et al

Examiner

Ungar

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Sep 11, 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires three months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: The proposed amendments raise the issue of scope of enablement under 35 USC 112, first para in that the claims no longer require that the glioma cells comprise an IL13-specific receptor

3. ☒ Applicant's reply has overcome the following rejection(s):
If the amendment were to be entered, overcomes rejections of claims 1,2,4-6,14-22 and 18-22 under 35 USC 112

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none

Claim(s) objected to: none

Claim(s) rejected: 1, 2, 4-6, and 14-22

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

10. ☐ Other: _____

SUSAN UNGAR, PH.D.
PRIMARY EXAMINER

Art Unit: 1642

1. If the amendment were to be entered, claims 1, 2, 4-6 and 14-22 would still be rejected under 35 USC 103 for the reasons previously set forth in Paper No. 24, Section 4, pages 2-5.

Applicant argues that the Debrinski abstract was never removed as a prior art reference. The argument has been considered but have not been found persuasive because, although Examiner did not specifically state that the reference was removed as prior art, the Examiner had clearly withdrawn the Debrinski abstract as prior art as shown in Paper No. 24 wherein Examiner stated that even without the confirmation in the Debinski paper, the invention would have been obvious for the reasons set forth therein and previously. Further, Examiner addressed the issue in the telephone interview of May 24, 2002 wherein Examiner stated that "Although Examiner did not explicitly state that Applicant had overcome the Debinski Abstract as prior art", the rejections were maintained because even with the withdrawal of the Debinski Abstract as prior art, the invention was obvious for the reasons set forth in Section 5.

Applicant requests a statement that the Abstract was removed as a prior art reference and requests withdrawal of the rejection of Section 5 because it would be identical to the section 4 rejection absent the availability of Abstract as a prior art reference.

In response, Examiner states that the Debinski Abstract was removed as a prior art reference by the declaration filed under 37 CFR. 1.132, filed February 1, 2002. Further, given that the rejection of Section 4 is identical to the rejection of

Art Unit: 1642

Section 5, absent the availability of Abstract as prior art, the rejection under Section 5 is withdrawn.

Applicant argues that (a) none of the references teach IL13R expression *in vivo* or *in situ*, rather, *in vitro* data is presented and therefore there is no reasonable expectation of success, (b) given the cited references, the invention would be obvious to try and the references do not provide motivation or a reasonable expectation of success, (c) *in vitro* data of the references is not enabling and does not support a reasonable expectation of success and nowhere has the Examiner provided factual support for the proposition that glioma cells *in situ* express the same type and level of receptors as do the explant cells, (d) the Debinski explant cells were processed in order to dissociate them which process the glioma cells *in situ* would not have been exposed to. Further, the cells were cultured in a nonhuman medium for at least several hours, (e) it would not be expected that administering IL13 receptor-targeting cytotoxins would kill or reduce the growth rate of glioma tumor cells *in situ*, (f) even with the addition of the Sashira reference, the claimed invention cannot be considered *prima facie* obvious for the reasons previously set forth.

The arguments have been considered but have not been found persuasive because (a') Applicant reiterates previous arguments, for the reasons previously set forth in Paper No. 24, page 4, "it is clear that one of skill in the art would have been motivated to treat for the reasons of record and would have believed that it is more likely than not that the hIL13 receptor is an appropriate target for the treatment of brain cancers, (b') in response to applicant's argument that the rejection is based

Art Unit: 1642

upon an "obvious to try" scenario, it is clear in the rejection that one of ordinary skill in this art would have been motivated to, and would have expected to, successfully apply the combined teachings of the references for the reasons of record, (c') MPEP 2164.02 specifically states in part that, as drawn to the correlation of *in vitro* data and *in vivo* efficacy, that the correlation is dependent upon the state of the prior art and that if the art is such that a particular model is recognized as correlating to a specific condition then it should be accepted as correlating and further the courts have found that a rigorous or an invariable exact correlation is not required (see *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747, Fed. Cir. 1985). It is clear for the reasons set forth previously that the art is such that the particular models used, which include the primary explant cells which were known to overexpress the claimed receptor, would have been accepted as correlating even if an invariable exact correlation had not been made, (d') dissociation of primary cells in order to plate them for the purpose of characterizing the primary cells was conventional in the art at the time the invention was made, it would not have been expected that the process described or the short term incubation would have materially affected the surface constituents of the primary explant cells, (e') given the teaching of the combined references along with the conventional nature of intra tumoral injection at the time the invention was made, the claimed invention is obvious for the reasons of record, (f') the invention is obvious for the reasons set forth previously and above.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER